

## **Phase II biomarker-driven study of ruxolitinib demonstrates effectiveness of JAK/STAT targeting in T-cell lymphomas**

### **Supplemental Data**

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## Supplemental methods: Multispectral immunofluorescence

### Multiplex Tissue Staining and Imaging

Primary antibody staining conditions were optimized using standard immunohistochemical staining on the Leica Bond RX automated research stainer with DAB detection (Leica Bond Polymer Refine Detection DS9800). Using 4  $\mu$ m formalin-fixed, paraffin-embedded tissue sections and serial antibody titrations, the optimal antibody concentration with the highest visual signal to noise ratio was determined followed by transition to a seven-color multiplex assay with equivalency. Optimal primary antibody stripping conditions between rounds of the seven-color assay were determined following 1 cycle of tyramide deposition followed by heat-induced stripping (see below) and subsequent chromogenic development (Leica Bond Polymer Refine Detection DS9800) with visual inspection for chromogenic product with a light microscope (TH). Multiplex assay antibodies and conditions are described in the table below.

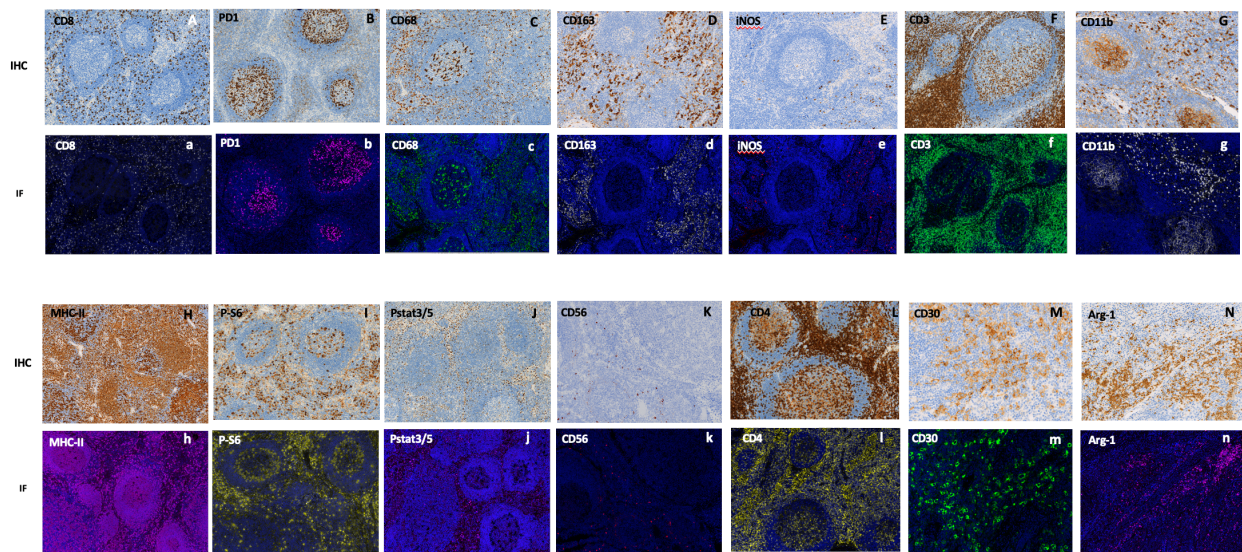
Panel	Opal520	Opal540	Opal570	Opal620	Opal650	Opal690	DAPI
<b>Panel 1</b>	CD3	CD68	PD-1	Pstat3/5	CD8	P-S6 cocktail	Hoechst
<b>Panel 2</b>	CD3	CD68	CD4	Pstat3/5	CD8	P-S6 cocktail	Hoechst
<b>Panel 3</b>	CD3	CD68	CD30	Pstat3/5	CD8	P-S6 cocktail	Hoechst
<b>Panel 4</b>	CD68	CD56	CD3	Pstat3/5	CD8	P-S6 cocktail	Hoechst
<b>Panel 5</b>	CD68	INOS	Arg-1	CD163	CD11b	MHC-II	Hoechst
Antigen		Antibody Clone		Manufacturer		Concentration	
<b>CD68</b>		PG-M1		Dako		1.5 $\mu$ g/ml	
<b>iNOS</b>		13F5.1		Millipore		1:5k	
<b>Arg-1</b>		D4E3M		CST		0.18 $\mu$ g/ml	
<b>CD163</b>		10D6		Leica		0.375 $\mu$ g/ml	
<b>CD11b</b>		D6X1N		CST		0.02 $\mu$ g/ml	
<b>MHC Class II</b>		TAL 1B5		Invitrogen		0.2ug/ml	
<b>CD4</b>		EPR6855		Abcam		0.07 $\mu$ g/ml	
<b>CD56 (RTU)</b>		MRQ-42		Cell MARQUE		1:2	
<b>CD8</b>		C8/114B		Cell Signaling		0.125 $\mu$ g/ml	
<b>CD3</b>		BC33		Biocare		1:200	
<b>CD30</b>		E4L4I		CST		1.62ug/ml	
<b>PD-1</b>		abcam		EPR4877		0.5 $\mu$ g/m	
<b>p-stat3 Tyr 705</b>		M9C6		Cell Signaling		1.05 $\mu$ g/ml	

<b>p-stat5 Tyr 694</b>	C11C5	Cell Signaling	7.66 µg/ml
<b>P-S6 Ser235/236</b>	D57.2.2E	Cell Signaling	0.2ug/ml
<b>P-S6 Ser240/244</b>	D68F8	Cell Signaling	0.06ug/ml

## Seven-color multiplex imaging assay

4 µm FFPE tissue sections were baked for 3 hrs. at 62 degrees Celsius in vertical slide orientation with subsequent deparaffinization performed on the Leica Bond RX followed by 30 minutes of antigen retrieval with Leica Bond ER2 followed by 6 sequential cycles of staining with each round including a 30-minute combined block and primary antibody incubation (Akoya antibody diluent/block ARD1001). For CD56 and CD68, detection was performed using a secondary horseradish peroxidase (HRP)-conjugated polymer (Akoya Opal polymer HRP Ms + Rb ARH1001; 10-minute incubation). Detection of all other primary antibodies was performed using a goat anti-mouse Poly HRP secondary antibody or goat anti-rabbit Poly HRP secondary antibody (Invitrogen B40961/2; 10-minute incubation). The HRP-conjugated secondary antibody polymer was detected using fluorescent tyramide signal amplification using Opal dyes 520, 540, 570, 620, 650 and 690 (Akoya FP1487001KT, FP1494001KT, FP1488001KT, FP1495001KT, FP1496001KT, FP1497001KT). The covalent tyramide reaction was followed by heat induced stripping of the primary/secondary antibody complex using Perkin Elmer AR9 buffer (AR900250ML) and Leica Bond ER2 (90% ER2 and 10% AR9) at 100 degrees Celsius for 20 minutes preceding the next cycle. After 6 sequential rounds of staining, sections were stained with Hoechst (Invitrogen 33342) for 10min to visualize nuclei and mounted with ProLong Gold antifade reagent mounting medium (Invitrogen P36930). Equivalency between single-marker optimized antibody IHC developed with 3, 3'-diaminobenzidine (DAB) and multiplexed 7-color immunofluorescence on normal lymph nodes, lymphoma, and pancreatic ductal adenocarcinoma (PDAC) is shown in the figure below.

Figure: Equivalency between single-marker optimized antibody IHC developed with 3, 3'-diaminobenzidine (DAB) on lymph nodes (A-L), lymphoma (M), PDAC (N) with multiplexed 7-color immunofluorescence on lymph nodes (a-l), lymphoma (m), PDAC (n). The immunofluorescent images represent individual marker position within the 7-color assay performed.



### **Multispectral imaging, spectral unmixing and cell segmentation**

Seven color multiplex stained slides were imaged using the Vectra Multispectral Imaging System version 3 (Perkin Elmer). Scanning was performed at 20X (200X final magnification). Filter cubes used for multispectral imaging were DAPI, FITC, Cy3, Texas Red and Cy5. A spectral library containing the emitted spectral peaks of the fluorophores in this study was created using the Vectra image analysis software (Perkin Elmer). Using multispectral images from single-stained slides for each marker, the spectral library was used to separate each multispectral cube into individual components (spectral unmixing) allowing for identification of the seven marker channels of interest using Inform 2.4 image analysis software. Images were exported to Indica Labs Halo image analysis platform and cell segmentation and signal thresholding was performed separately on each case using a supervised algorithm performed by a pathologist.

### **Multispectral immunofluorescence lymphoma panels and analysis**

Slides were stained with DAPI plus antibodies against CD3, CD8 and the macrophage marker CD68. Depending on the disease an antibody was added for PD1 (for AITL and PTCL cases), CD30 (for ALCL cases), CD56 (for NKTCL cases) or CD4 (for MF and T-PLL cases). Using the HALO software, areas of TCL involvement within biopsy slides were manually defined during image analysis based on mIF, compared to clinical IHC, and confirmed by two investigators (P.G., P.D.). For pS6 and pSTAT3/5, we calculated the quantity of both total and tumor cells expressing that marker.

Supplemental Table 1.

CLINICAL INFORMATION					PHOSPHO STAINING				NEXT GENERATION SEQUENCING											p56 and pSTAT3-5 mIF (Pre-Rux)				
STUDY ID	Histology	Cohort	Best Response	Timepoint	Type of Biopsy	pSTAT3	pSTAT5	Timepoint2	Type of Biopsy	Mutations	Specific Mutation	Copy Number Alterations	Comments	Type of Biopsy3	Tumor cells defined	%tumor cells/total cells	pSTAT3-5% positive cells	% tumor + pSTAT3-5/ total tum cells	p56% positive cells	% tumor + p56/ total tum cells				
7	PTCL, NOS	1	PR	Pre-Rux	Lymph Node (R Paratracheal)	<5%	Not Done	at diagnosis	Lymph Node (R Paratracheal)	ATM, CUX1, ERBB4, JAK3, KSR2, SETD2, STAT5B	ATMR457 (0.58), CUX1P1376L (0.40), ERBB4V675F (0.33), JAK3M511 (0.28), KSR2R665W (0.34), SETD2G1690R (0.36), STAT5B1628S (0.76)	CEBBP (Loss, FC: -1.6), NF2 (Gain, FC: 1.4), EP300 (Gain, FC: 1.4), SOCS1 (Loss, FC: -1.7), CHK2 (Loss, FC: -1.4), XBP1 (Loss, FC: -1.4)		mediastinal mass	CD3+, CD56+, CD4-	35.96	4.75	2.70	0.00	0.00				
26	PTCL, TFH	1	POD	Pre-Rux	Skin Punch (L Dorsal Foot)	90%	80%	Pre-Rux	Skin Punch (L Dorsal Foot)	DNMT3A, TET2, TP53, TET3, STAT3, JAK1	DNMT3AW860Mfs*4 (0.48), TET2S158P* (0.31), TET2S1050P* (0.36), TP53K331L_splice (0.61), TET3G423Mfs*126 (0.69), STAT3E1646H (0.32), JAK1G1097V (0.69)	TET3 (Loss, FC: -1.5)		Skin Punch	CD3+, PD1+	16.58	29.82	52.46	49.37	54.02				
12	T-PLL	1	PR	At Diagnosis/Pre MTX and Pre Rux	Tissue Punch (Tongue)	0%	0%	Pre-Rux	Blood	ATM, EED, SH2B3, STAT5B	ATMX2950_Splice (0.97), EEDL45K (0.97), SH2B3G214E (0.58), STAT5B1628S (0.91)	FGFR1 (Gain, FC: 1.6), CDKN1B (Loss, FC: -1.8), ATP9A1P (Gain, FC: 1.8), ATP9B1B2 (Loss, FC: -1.8), ESCD2 (Loss, FC: -1.9), ETV6 (Loss, FC: -1.8), CDRB (Loss, FC: -1.4), FLT3 (Loss, FC: -1.4), FLT3 (Loss, FC: -1.4)												
41	PTCL, NOS	1	SD	Pre-Rux	Bone Marrow	0	0	Pre-Rux	Bone Marrow	HGF, AKT3, SETD2, STAT5B, SETD2	HGF5510P* (0.06), AKT3A406P (0.11), SETD2V1671C (0.49), STAT5BNG42H (0.86), SETD2S311P* (0.40)	None												
44	T-PLL	1	PR	At Diagnosis/Pre-Rux	Bone Marrow	0	90%	At Diagnosis/Pre-Rux	Blood	ATM, EED, GRIN2A, KSR2, STAT5B	EEDN1945 (0.16), GRIN2AT308M (0.13), GRIN2AT1362I (0.34), KSR2R267Q (0.34), STAT5BNG42H (0.22), STAT5BQ706L (0.09), ATMK213L_splice (0.45)	None												
49	T-PLL	1	PR	At Diagnosis	Bone Marrow	0%	90%	At Diagnosis	Bone Marrow	JAK3, KMT2A	JAK3K563_C365del (0.36), KMT2AR2760S (0.42)	ARID1A (Loss, FC: -1.8), BRAF (Loss, FC: -1.7), MGAAM (Loss, FC: -1.7), E2F2 (Loss, FC: -1.7), SAMHD1 (Loss, FC: -1.5), KMT2C (Loss, FC: -1.4)												
53	T-PLL	1	POD	On Study (Ruxofitinib)	Bone Marrow	0	0	At Diagnosis	Blood	ATM, JAK3, SAMHD1	ATMD1082H (0.42), ATMK3030R (0.48), JAK3M511 (0.08), JAK3V674A (0.27), JAK3M511 (0.03), SAMHD1M385R (0.43)	RAD21 (Amplification, FC2.1), MYC (Amplification, FC2.1), PPP2R1A (Amplification, FC2.1), U2AF2 (Amplification, FC2.1), NBN (Amplification, FC2.1), RUNX1T1 (Amplification, FC2.2), UBR5 (Amplification, FC2.2), FGFR1 (Amplification, FC2.3)												
11	HSCTCL	1	PR	Pre-Rux	Bone Marrow	5%	Not Done	Pre-Rux	Bone Marrow	KRAS, SETD2, STAT5B, SETD2	KRASG12V (0.18), SETD2L1804S (0.25), STAT5BNG42H (0.27), SETD2R400P* (0.28)	None												
54	MEITL	1	SD	Pre-Rux	Left Colon	5%	70% (High Background)	Pre-Rux	Spleen and Distal Pancrease (Flow)	STAT5B	STAT5BNG42H (0.37)	None												
23	pcALCL	1	CR	Unknown	Unknown	10%	90%	Unknown	Skin Punch (L Upper Lip)	STAT3 See Additional Excel for full list	STAT3E638K (0.11) See Additional Excel for full list	None												
37	ALCL, ALK-	1	POD	Pre-Rux	Lymph Node (L External iliac)	10%	Not Done	Pre-Rux	Lymph Node (L External iliac)	TNFAIP3, ALK, AXL, EPHA7, FAT1, STAT3	TNFAIP3L126Gfs*84 (0.46), ALKG1135 (0.50), AXLR474Q (0.41), EPHA7S425N (0.40), FAT1P4246L (0.41), FAT1S3446R (0.41), STAT3Y640P* (0.43), TNFAIP3K212_splice (0.46)	SDHB (Amplification, FC: 2.2), HNRK (Amplification, FC: 2.2), MDM4 (Amplification, FC2.9), MTOR (Amplification, FC: 3.1), CD58 (Deletion), STAG1 (Deletion), DUSP22 (Gain, FC: 1.7), IRF4 (Gain, FC: 1.9), POTT1 (Loss, FC: -1.8), TP53 (Loss, FC: -1.8), ALDH12B (Loss, FC: -1.8), AURKB (Loss, FC: -1.8), GNB1 (Loss, FC: -1.8), TNFRSF14 (Loss, FC: -1.8), ID3 (Loss, FC: -1.7), ARID1A (Loss, FC: -1.7), ARID1A (Loss, FC: -1.7), SYK13 (Loss, FC: -1.7), ARID4B (Loss, FC: -1.4), AKT3 (Loss, FC: -1.4)												

Supplemental Table 1 continued

CLINICAL INFORMATION					PHOSPHO STAINING				NEXT GENERATION SEQUENCING										p56 and pSTAT3-5 mIF (Pre-Rux)				
STUDY ID	Histology	Cohort	Best Response	Timepoint	Type of Biopsy	pSTAT3	pSTAT5	Timepoint2	Type of Biopsy	Mutations	Specific Mutation	Copy Number Alterations	Comments	Type of Biopsy3	Tumor cells defined	%tumor cells/total cells	pSTAT3-5% positive cells	% tumor + pSTAT3-5/ total tum cells	p56% positive cells	% tumor + p56/ total tum cells			
59	CTCL MF	1	POD	Pre-Rux	Skin Punch (R Anterior Upper Arm)	20%	100%	Pre-Rux	Skin Punch (R Anterior Upper Arm)	IDH1, JAK3, SAMHD1, ARID1A, EPAS, FAT1, FAT1, HRAS, KMT2D, NCCR2, NFE2L2, NTRK5, SETD7, TET1, TET3, UBR5	IDH1R132C (0.41), JAK3G571W (0.46), SAMHD1C341_L347N e1 (0.75), ARID1AS458F (0.36), EPASD267N (0.45), FAT1L1506C (0.39), FAT1E2874E (0.41), HRASG56N (0.41), KMT2DP3315S (0.08), NCCR2P2367S (0.36), NFE2L2P148S (0.41), NTRK5P71S (0.08), SETD7G24R (0.44), TET1V135K (0.43), TET3L121V (0.39), UBR5S547V (0.42)	KDM6A (Deletion, FC -3.0), CBL (Loss, FC -1.6), CHEK1 (Loss, FC -1.6), KMT2A (Loss, FC -1.4), ATPEAP1 (Amplification, FC: 2.0)											
60	T-LGL	1	SD+6 mo	Pre-Rux	Bone Marrow	20%	0% (High background)	Pre-Rux	Bone Marrow	EGFR, STAT3	EGFR4864V (0.26), STAT3K658R (0.27)	None											
5	T-LGL	1	PR	Pre-Rux	Bone Marrow	80%	90%	Pre-Rux	Blood	STAT3 and ML12	STAT3Y640F (0.14), ML12G3021S*10 (0.13)	None	Notes: VUS results- SMOR726Q (0.51), FLONA163T (0.14), SETBP1K1108R (0.48), KDRK275Q (0.52), EPHE1R367H (0.06), MAP3K6P46L (0.52), ARPS15R (0.11), PCLD0197H (0.49), GPR124T748 (0.54), KDM5AV1208E (0.50), SPENP261_A1262del (0.47), CDKN2CL107V (0.49)										
15	AITL	1	SD+6 mo	N/A	N/A	Not Done	Not Done	At Diagnosis	Lymph Node (R Axillary)	STAT3	STAT3Y640F (0.13)	None											
19	T-LGL	1	POD	N/A	N/A	Not Done	Not Done	Pre-Rux	Blood	ARID1A, BTK, DDX3X, FBXW7, JAK2	ARID1AQ13344dup (0.47), BTKG521V (0.13), DDX3N551K5*4 (0.13), FBXW7Q76L (0.50), JAK2R487C (0.50)	None											
22	T-PLL	1	SD+6 mo	N/A	N/A	Not Done	Not Done	At Diagnosis/Pre-Rux	Blood	SAMHD1, ATM, EED, EPAS, JAK1, JAK3, SAMHD1, SETD4	SAMHD1L178* (0.40), ATMCC021V (0.80), EEDK400N (0.68), EPASR543C (0.43), JAK1Y652H (0.24), JAK3M511 (0.03), JAK3A374V (0.06), JAK3V74A (0.04), JAK3M511 (0.02), SAMHD1D424E (0.44), SETD4H122V (0.44)	CDKN1B (Loss, FC -1.9), EED (Loss, FC -1.6), MRE11A (Loss, FC -1.6), BIRC3 (Loss, FC -1.6), ATM (FC -1.6)											
24	T-PLL	1	POD	N/A	N/A	Not Done	Not Done	Pre-Rux	Blood	ATM, EZH2, MYCN, STAT5B	ATMG2765V (0.72), EZH2R25P (0.22), MYCNP57R (0.08), STAT5BQ475N (0.13), STAT5ATK628S (0.32), STAT5BKV112E (0.07)	None											
27	HSTCL	1	SD	N/A	N/A	Not Done	Not Done	Pre-Rux	Liver Mass	STAT5B	STAT5BN642H (0.23), STAT5B7628S (0.28)	None											
28	CTCL	1	SD	N/A	N/A	Not Done	Not Done	Pre-Rux	Skin	ARID1B, ATM, ATRX, CBL, FAS, GNL3, HMBP2, KDM5A, KMT2D, MET, MLH1, MYB, SLC4A2, SMARCA4, SOS1, STAT3	ARID1BE1370* (0.08), ATMF897 (0.48), ATRXSL205F (0.12), CBL (0.14), FASL224* (0.11), GEN1D722N (0.10), GUP1485F (0.11), HMBP2104F (0.12), KDM5ALV79F (0.14), KMT2DP2333S (0.46), KMT2DP2277S (0.11), METE100R (0.23), MHL1G67H (0.49), MYB (0.10), SLC4A2P317L (0.16), SMARCA4P513L (0.09), SOS1T37A (0.50), STAT3P715L (0.18)	CSF3R (Loss), XPO1 (Loss), HFE (Loss), HST1H8B (Loss), HST1H3C (Loss), ID4 (Loss), PRSS1 (Loss), CDKN2A (Loss), MTAP (Loss), C17ORF70 (Gain), RPTOR (Gain)	Additional copy number alterations: CNV analysis shows focal loss of CDKN2A (p56), which was reported as a single copy deletion, but may, in fact, represent a two-copy deletion, although it is somewhat difficult to determine this with certainty										
36	T-PLL	1	SD	N/A	N/A	Not Done	Not Done	Pre-Rux	Unknown	JAK3	JAK3V722I (0.46)	None											
6	AITL	2	PR	Pre-Rux	Abdominal Wall Nodule	70%	Not Done	At Diagnosis	Lymph Node (L Groin)	TET2, DNMT3A, TP53	TET2Q15137* (0.12), DNMT3AIG61M (0.10), TET2N1610H*16 (0.11)	None		Lymph Node (L Groin)	CD3+ PD1+	10.49	2.63	3.88	6.61	3.37			
10	T-PLL	2	POD	Pre-Rux	Skin Punch (R Palm)	40%	90%	N/A	N/A	N/A	N/A	N/A		Skin Punch	CD4+ CD3+ CD8-	42.89	47.72	67.93	15.11	10.80			
9	PTCL NOS	2	CR	Pre-Rux	R Psoas Muscle	30%	Not Done	Pre-Rux	R Psoas Muscle	B2M, BRCA2, FAS, PRDM1	B2ML13R (0.24), BRCA2V3290A (0.22), FASG206S (0.33), PRDM1X5B2_splice (0.29)	None		R Psoas Muscle	CD2+, CD8-, PD-1+	9.07	12.03	15.61	23.48	21.95			
1	AITL	2	POD	Pre-Rux	Lymph Node (L Retroperitoneal)	70-80%	Not Done	Pre-Rux	Lymph Node (L Retroperitoneal)	IGH2, TET2, RHOA	IGH2R172S (0.05), TET2R1216 (0.08), TET2G72S (0.05), RHOAG17V (0.06)	None		Lymph Node	CD3+, PD1+ CD8-	44.17	7.23	2.49	68.59	57.02			
13	CTCL	2	POD	Pre-Rux	Skin Punch (R Upper Outer Quadrant of Breast)	50-60%	Not Done	Pre-Rux	Skin Punch (R Upper Outer Quadrant of Breast)	TP53, RPTOR, BRD4, MYC, PRK3C2G	TP53Y205N (0.03), RPTORQ292C*121 (0.56), BRD4M1152I (0.05), MYOP327A (0.08), PRK3C2V1188M (0.09)	None	Structural Variants - SRSF2_NIN12 Translocation										

Supplemental Table 1 continued

CLINICAL INFORMATION					PHOSPHO STAINING				NEXT GENERATION SEQUENCING					p56 and pSTAT3-5 mIF (Pre-Rux)						
STUDY ID	Histology	Cohort	Best Response	Timepoint	Type of Biopsy	pSTAT3	pSTAT5	Timepoint2	Type of Biopsy	Mutations	Specific Mutation	Copy Number Alterations	Comments	Type of Biopsy3	Tumor cells defined	%tumor cells/total cells	pSTAT3-5% positive cells	% tumor + pSTAT3-5/ total tum cells	p56% positive cells	% tumor + p56/ total tum cells
21	AITL	2	CR	Pre-Rux	Lymph Node (R Inguinal Node)	100%	80%	Pre-Rux	Lymph Node (R Axillary)	TET2, VAV1, SOCS1, PAK5, FAS	TET2P18H4 (0.26), TET2P55H4*6 (0.24), VAV1G106D (0.06), SOCS1A5 (0.11), PAK5Y7F (0.09), FASN252D (0.12)	None								
29	SPFCL	2	SD=6 mo	Pre-Rux	Skin Punch (R Anterior Upper Arm)	60%	90%	Pre-Rux	Skin Punch (L Anterior Upper Arm)	no mutations	N/A	N/A								
31	PTCL, NOS	2	NR for Response	Unknown	Unknown	90%	failed	N/A	N/A	N/A	N/A	N/A								
34	CTCL	2	POD	Unknown	Unknown	>50%	Not Done	N/A	N/A	N/A	N/A	N/A								
42	PTCL, NOS	2	POD	Pre-Rux	Bone Marrow	80-100%	Not Done	At Diagnosis	Lymph Node (Cervical)	TET2, FLT3, ARID2, TET3	TET2C137B* (0.30), FLT3R312 (0.48), ARID2S101B* (0.31), TET3W1504* (0.32)	BCOR (Deletion, FC-2.5), PTEN (Deletion, FC-2.4), GNAQ2 (Loss, FC-1.6), NTRK2 (Loss, FC-1.6), SYK (Loss, FC-1.6), FANCC (Loss, FC-1.6), PDCD1 (Loss, FC-1.5), PTCH1 (Loss, FC-1.5), SP540 (Loss, FC-1.5), HDAC4 (Loss, FC-1.5)								
45	PTCL, NOS	2	POD	Unknown	Unknown	50%	30%	N/A	N/A	N/A	N/A	N/A								
52	AITL	2	PR	At Diagnosis	Lymph Node (R Axillary)	60%	25%	Pre-Rux	Blood	CTNNB1, RHGA	CTNNB1T41A (0.05), RHGAG17V (0.07)	None								
55	PTCL, NOS	2	POD	Unknown	Unknown	>50%	0%	N/A	N/A	N/A	N/A	N/A								
56	AITL	2	POD	Post-Rux	Unknown	>70%	0%	N/A	N/A	N/A	N/A	N/A								
58	CTCL, MF	2	POD	Pre-Rux	Skin Punch (R Upper Back)	90%	80%	Pre-Rux	Skin Punch (R Dorsal Forearm)	no mutations										
20	AITL	3	POD	Pre-Rux	Duodenum	20%	Not Done	Pre-Rux	Spleen	TET2, ATM	TET2L719Cfs*32 (0.29), TET2G79Ffs*13 (0.24), ATMR300B (0.07), ATMR300C (0.19)			duodenum	CD3+, PD+	35.92	5.34	6.36	38.68	38.89
40	GD-TCL	3	SD	Pre-Rux	Skin Punch (L lower leg superior/inferior)	20%	Not Done	Pre-Rux	Bone Marrow	no mutations	N/A	N/A		Skin Punch	CD56+, CD3+, CD8-	30.23	2.35	0.63	48.30	27.27
3	ALCL, ALK-	3	POD	Pre-Rux	Skin Punch (L Lower Abdomen)	<5%	Not Done	Pre-Rux	Skin Punch (L lower anterior chest)	TP53, TET2, RARA, FOXL2, FLT3, ERBB4, DNMT3A	TP53P35Q (0.63), TET2 (c.3595-2A>G) (0.48), RARAG434V (0.39), FOXL2A304T (0.36), FLT3E177K (0.62), ERBB4C269R (0.39), DNMT3A647P (0.43)	PTEN (Deletion, FC-2.8), ZFHQ3 (Deletion, FC-2.0), CIC (Gain, FC-1.7), RECQL4 (Amplification, FC-2.0), PIK3CD (Amplification, FC-2.1), MTOR (Amplification, FC-2.1)		Skin Punch	CD30+, CD3+ CD8-	48.91	3.71	0.54	63.16	63.77
4	CTCL, MF	3	SD	Pre-Rux	Skin Punch (L Lower Anterior Chest)	20%	90%	Pre-Rux	Skin Punch (L Lower Anterior Chest)	DNMT3A, EP300, TSC2, AK1, EP300, RAD50, RGS1, SMO, STK11, TSC2	DNMT3A R271S*4, DNMT3A R326P, EP300Q226Rdel, TSC2P1510del, AK1S400P, EP300P261S, RAD50R105C, RGS1P128S, SMOV154M, STK11A241P, TSC2R1706H	None								
14	T-LGL	3	PR	Pre-Rux	Bone Marrow	Not morphologically evident	Not morphologically evident	Pre-Rux	Blood	no mutations										
16	ATLL	3	POD	N/A	N/A	Not Done	Not Done	Post-Rux	Unknown	no mutations	N/A	None								
17	ATLL	3	POD	N/A	N/A	Not Done	Not Done	Post-Rux	Unknown	PCMTD1, CD24, CD58	PCMTD1K277X (0.085), CD24C32C (0.045), CD58S1995X (0.037)	None								
18	ATLL	3	POD	N/A	N/A	Not Done	Not Done	Post-Rux	Unknown	No mutations	N/A	None								
30	PTCL, NOS	3	POD	Unknown	Unknown	0%	40%	Unknown	Unknown	No JAK/STAT mutations See Additional Excel for full list	No JAK/STAT mutations See Additional Excel for full list	None								
32	PTCL, NOS	3	POD	N/A	N/A	Not Done	Not Done	N/A	N/A	N/A	N/A	N/A								
33	CTCL	3	PR	Unknown	Unknown	20%	80%	Unknown	Unknown	No JAK/STAT mutations See Additional Excel for full list	No JAK/STAT mutations See Additional Excel for full list	None								
35	PTCL, TH	3	POD	N/A	N/A	Not Done	Not Done	N/A	N/A	N/A	N/A	N/A								
39	PTCL, NOS	3	POD	Pre-Rux	Bone Marrow	<5%	0%	At Diagnosis	Lymph Node (L Supraclavicular)	TP53, FAS, EPHA3, KDR, KMT2C, PLCG1	TP53P278fs*67 (0.74), FASN302fs*57 (0.66), EPHA3R380fs*19 (0.25), KDR R791G (0.72), KMT2D H3390 (0.27), PLCG1G1015S (0.46), PLCG1E1163K (0.42)									
48	T-LGL	3	SD=6 mo	Pre-Rux	Bone Marrow	0%	0%	Pre-Rux	Blood	no mutations	N/A	N/A								
50	PTCL, NOS	3	POD	N/A	N/A	Not Done	Not Done	N/A	N/A	N/A	N/A	N/A								
51	PTCL, NOS	3	POD	Pre-Rux	Lymph Node (R Groin)	15%	90%	Pre-Rux	Lymph Node (R Groin)	TET2, EPHA3, KMT2D, PLCG2, POT1, CD58, SOCS1	TET2Q769* (0.10), TET2Q881* (0.15), EPHA3Y474C (0.21), KMT2D V1340A (0.13), PLCG2T813S (0.06), POT1T105K (0.09), CD58Q10K* (0.15), SOCS1G78P* (0.24)	None								
57	ALCL, ALK-	3	POD	At Diagnosis	Lymph Node (L Groin)	0%	0%	At Diagnosis	Lymph Node (L Groin)	SOCS1	SOCS1T100Nfs*17 (0.08)	None								

Supplemental Table 2. Efficacy for nodal TCL (PTCL, NOS, AITL, and ALCL) according to cohort

<b>Cohorts</b>	<b>Total Treated</b>	<b>Total Evaluable for Response</b>	<b>ORR</b>	<b>CBR</b>	<b>CR</b>	<b>PR</b>	<b>SD&gt;6 mo</b>
<b>Cohort 1</b>	<b>5</b>	<b>5</b>	<b>1 (20%)</b>	<b>2 (40%)</b>	<b>0 (0%)</b>	<b>1 (20%)</b>	<b>1 (20%)</b>
<b>Cohort 2</b>	<b>10</b>	<b>9</b>	<b>4 (44%)</b>	<b>4 (44%)</b>	<b>2 (22%)</b>	<b>2 (22%)</b>	<b>0 (0%)</b>
<b>Cohort 3</b>	<b>9</b>	<b>9</b>	<b>0 (0%)</b>	<b>0 (0%)</b>	<b>0 (0%)</b>	<b>0 (0%)</b>	<b>0 (0%)</b>
<b>Total</b>	<b>24</b>	<b>23</b>	<b>5 (22%)</b>	<b>6 (26%)</b>	<b>2 (9%)</b>	<b>3 (13%)</b>	<b>1 (4%)</b>
<b>p (cohorts 1&amp;2 versus 3)</b>			<b>ORR, p=0.12</b>	<b>CBR, p=0.048</b>			